

## REMARKS

### *Amendments*

The amendment to the Specification merely inserts the related application information. The claims are amended to delete the grammatically redundant “R”. These amendments do not change the scope of the claims and introduce no new matter.

### *35USC112, second paragraph*

Claims 65-115. The recited “R” is grammatically unnecessary and has been deleted.

### *35USC102(b)*

Claim 62. Krishna et al. (Aug. 1998, Journal of Medicinal Chemistry 41(18):3477-92; full article attached) studied the effect of ring size, oxidation state and redox midpoint potentials of five or six-membered secondary nitroxides historically used as biophysical probes. The intermediate reduced forms of Krishna’s nitroxides are the corresponding five or six-membered secondary hydroxylamines (e.g. compounds 1b, 2b, 5b, 6b, 9b, 11b-17b, 19b, 22b, 23b, 25b-27b, 29b, 36b-38b, 40b, 42b, 48b, 52b, 53b, and 55b; Krishna (1998) p.3478, col.2, lines 30-32).

Our claims require primary N-hydroxylamines, which are structurally and functionally different from the cyclic secondary hydroxylamines studied by Krishna.

### *35USC103(a)*

Claims 62-131. Krishna et al. (1998, *supra*) studied the effect of ring size, oxidation state and redox midpoint potentials of five or six-membered secondary nitroxides historically used as biophysical probes. The intermediate reduced forms of Krishna’s nitroxides are the corresponding five or six-membered secondary hydroxylamines (e.g. compounds 1b, 2b, 5b, 6b, 9b, 11b-17b, 19b, 22b, 23b, 25b-27b, 29b, 36b-38b, 40b, 42b, 48b, 52b, 53b, and 55b; Krishna (1998) p.3478, col.2, lines 30-32).

Our claims require primary N-hydroxylamines, which are structurally and functionally different from the cyclic secondary hydroxylamines studied by Krishna, especially as they relate to biological systems. By functionalizing a second proton, particularly in a cyclical carbon ring, cyclic secondary amines present substantially different chemical reactivities, in part by reducing the availability (reactivity or nucleophilicity) of the free electron pair of the Nitrogen. This can

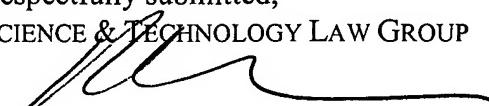
be seen, for example, in the strikingly different redox potentials of secondary and primary hydroxylamines. Primary hydroxylamines have redox potentials in the 300 mV range (see Fig.3 of Tamilmani et al., 2003, DuPont Electronic Technology, <http://www.ekctech.com/images/feauture-stories/MRS-Interaction%20between%20ceria%20and%20Hydroxylamine.pdf>, enclosed), near that of the intracellular reducing potential (e.g. Sies, et al., 1977, Euro J Biochem 72, 301-7, abstract attached), whereas the cyclic secondary hydroxylamines of Krishna et al. provide redox potentials ranging from 722 to 960 mV (see, e.g. Krishna et al., 1992, PNAS USA 89, 5537-41, attached).

Krishna (1998) describes use of dozens of different compounds, but every one is a similar cyclic secondary nitroxide (and the corresponding hydroxylamines and amines). Krishna (1998) provides no suggestion or motivation to deviate from his teachings and employ a structurally and functionally distinct class of hydroxylamines, particularly since Krishna (1998) repeatedly reports that variation in redox potential across his reagents showed no significant correlation between protection and redox potentials (e.g. Krishna, 1998, at p.3488, col.2, line 41-45).

The Examiner is invited to call the undersigned if he would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

We petition for and authorize charging our Deposit Account No.19-0750 all necessary extensions of time. The Commissioner is authorized to charge any fees or credit any overcharges relating to this communication to our Dep. Acct. No.19-0750 (order B00-001-2).

Respectfully submitted,  
SCIENCE & TECHNOLOGY LAW GROUP

  
Richard Aron Osman, J.D., Ph.D., Reg. No. 36,627  
Tel: (650) 343-4341; Fax: (650)343-4342

- Encl. Krishna et al. (1998, Journal of Medicinal Chemistry 41(18):3477-92)  
Sies et al. (1977, Euro J Biochem 72, 301-7, abstract)  
Krishna et al. (1992, PNAS USA 89, 5537-41).  
Tamilmani et al. (2003, Dupont Electronic Technology, 6 p.)

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